A novel continuous arterial spin labeling approach for CBF measurement in rats with reduced labeling time and optimized signal-to-noise ratio efficiency

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Abstract
Objective To develop a continuous arterial spin labeling (CASL) perfusion imaging method for cerebral blood flow (CBF) measurement in rats with reduced spin-labeling length and optimized signal-to-noise ratio \( (SNR_f) \) per unit time.

Materials and methods In the proposed method, the longitudinal magnetization of brain tissue water in the imaging slice is prepared into a proper state before spin-labeling, and a post-tagging delay is employed after spin-labeling. The method was implemented on a 4.7 T small animal scanner. Numerical simulations and in vivo experiments were used to evaluate the performance of the method proposed.

Results With the proposed method, absolute CBF could be measured accurately from normal rat with a spin-labeling pulse as short as 400 ms, and yet employing the same formula as that used in the conventional CASL perfusion imaging method for calculation. The method also showed improved \( SNR_f \) per unit time over the conventional CASL perfusion imaging method and the pulsed arterial spin labeling perfusion imaging method FAIR.

Conclusion Compared to the conventional CASL perfusion imaging method, the proposed method would be advantageous for CBF measurement in small animals having short vascular transit time in terms of \( SNR_f \) per unit time and other benefits brought by shortened spin-labeling pulse.

Keywords Magnetic resonance perfusion imaging · Cerebral blood flow · Continuous arterial spin labeling · Signal-to-noise ratio efficiency · Rat

Introduction
Magnetic resonance perfusion imaging with arterial spin labeling (ASL) are widely used for non-invasive measurements of cerebral blood flow (CBF) under clinical settings and in experimental animals [1–4]. Two types of ASL techniques are currently available, continuous arterial spin labeling (CASL) and pulsed arterial spin labeling (PASL). In CASL, the blood water protons in the carotid arteries are labeled with a long (i.e., in the order of seconds) inversion/saturation pulse. In comparison, a relatively short labeling pulse (i.e., milliseconds to tens of milliseconds) is used in PASL, along with a slice-selective gradient, to label the longitudinal magnetization of the arterial blood water in a brain slab proximal, with respect to the direction of blood flow, to the imaging brain slice.

For perfusion imaging on small animals (i.e., rodents), CASL is often preferred because theoretically it provides higher signal-to-noise ratios (SNR) for CBF measurements than the PASL methods such as flow-sensitive alternating inversion recovery (FAIR) [5]. One problem with the conventional CASL technique is that, for the purpose of simplifying calculation of absolute CBF, the spin-labeling pulse has to be set long enough (i.e., 1.5–6 s) to ensure the longitudinal magnetization of brain tissue water in the imaging slice reaches a steady state after spin labeling [1]. This, however, could lead to some undesired consequences: 1) high specific adsorption rate (SAR), especially when CBF is measured repeatedly with a high temporal resolution, such as in fMRI.
studies, and 2) reduced SNR efficiency (i.e., SNR per unit time) for CBF measurement.

In this study, we developed a novel CASL perfusion imaging method, in which the length of the spin-labeling pulse can be reduced to as short as the vascular transient time (i.e., the time required for the water molecules in the arterial blood to travel from the labeling plane to the imaging slice), and yet the formula for calculating absolute CBF remains the same as that used in conventional CASL perfusion imaging [1]. The method was implemented on a 4.7 T small animal scanner and used to acquire quantitative CBF maps from normal rats. It was also shown that, for CBF measurement in rats, the proposed method can be advantageous over both the conventional CASL method [1] and the FAIR method in terms of SNR efficiency.

\[
\frac{dM_b}{dt} = \begin{cases} 
\frac{M_0 b(t) - M_b(t)}{T_{1b}} & - k_{for} M_b(t) + \frac{\lambda}{\gamma} M_0 b(t) - \frac{\lambda}{\gamma} M_b(t) \\
\frac{M_0 b(t) - M_b(t)}{T_{1b}} & - k_{for} M_b(t) - (2\alpha - 1) \frac{\lambda}{\gamma} M_0 b(t) - \frac{\lambda}{\gamma} M_b(t) \\
\frac{M_0 b(t) - M_b(t)}{T_{1b}} & - (2\alpha - 1) \frac{\lambda}{\gamma} M_0 b(t) - \frac{\lambda}{\gamma} M_b(t) \\
\frac{M_0 b(t) - M_b(t)}{T_{1b}} & + \frac{\lambda}{\gamma} M_0 b(t) - \frac{\lambda}{\gamma} M_b(t)
\end{cases}
\]

\[
\text{when } t < \delta \\
\text{when } \delta \leq t \leq \tau \\
\text{when } \tau \leq t \leq \tau + \delta \\
\text{when } \tau + \delta \leq t \leq \tau + w
\]

where \(\delta\) is the vascular transient time, \(\tau\) is the duration of the spin-labeling pulse and \(\tau \geq \delta\), \(w\) is the duration of the post-tagging delay (Fig. 1), \(T_{1b}\) is the intrinsic spin-lattice relaxation time of brain tissue water protons, \(f\) is the tissue perfusion rate (i.e., CBF), \(\alpha\) is the degree of spin-labeling in the imaging slice, \(\lambda\) is the brain:blood partition coefficient of water, \(k_{for}\) is the forward MT rate constant between brain tissue water protons and macromolecular protons. It is assumed that the macromolecular protons are completely saturated instantaneously by the spin-labeling pulse, and there is an instantaneous equilibrium among brain tissue water, arterial water and venous water (i.e., water being a freely-diffusible tracer). For simplicity, MT occurring after the spin-labeling period is ignored in Eq. 1.

Two scans are required to measure \(f\), one with spin labeling at the carotid arteries (i.e., \(\alpha \neq 0\)) and the other without (i.e., the control scan, \(\alpha = 0\)). In the control scan, \(M_b\) measured after the post-tagging delay \((M_{b}^{\text{con}})\) can be calculated by integrating Eq. 1 and with the boundary condition \(M_b(0) = r_0 M_b^0\), and

\[
M_b^{\text{con}}(\tau, r_0) = M_b^0 \left[ 1 - e^{-w/T_{\text{ins}}} + \frac{T_{1s}}{T_{\text{ins}}} e^{-w/T_{\text{ins}}} \left( 1 - e^{-\tau/T_{1s}} \right) \right. \\
\left. + r_0 e^{-w/T_{\text{ins}}} e^{-\tau/T_{1s}} \right].
\]

Materials and methods

Theory

Figure 1 shows a schematic representation of the pulse sequence for the proposed method. Before applying the spin-labeling pulse, the longitudinal magnetization of brain tissue water in the imaging slice \((M_b)\) is manipulated by an adiabatic slice-selective saturation (90°) pulse and an adiabatic slice-selective inversion (180°) pulse, the two of which are separated by a time interval \(w\). The concept of preparing \(M_b\) before spin-labeling is adopted from the ASL techniques with background suppression (e.g., making \(M_b = 0\) before spin labeling) [6,7]. In the proposed method, \(M_b\) is prepared into an exact state of \(r_0 M_b^0\) (i.e., \(-1 \leq r_0 \leq 0\)) before spin labeling (see below), where \(M_b^0\) is the equilibrium value of \(M_b\).

During the spin-labeling period, the spin-labeling pulse not only tags the water protons in the arterial blood, but also introduces magnetization transfer (MT) effect in the imaging slice. Using a two-compartment exchange model for MT and including the effects of CBF, the modified Bloch equations for \(M_b\) can be expressed as

\[
\frac{dM_b}{dt} = \begin{cases} 
\frac{M_0 b(t) - M_b(t)}{T_{1b}} & - k_{for} M_b(t) + \frac{\lambda}{\gamma} M_0 b(t) - \frac{\lambda}{\gamma} M_b(t) \\
\frac{M_0 b(t) - M_b(t)}{T_{1b}} & - k_{for} M_b(t) - (2\alpha - 1) \frac{\lambda}{\gamma} M_0 b(t) - \frac{\lambda}{\gamma} M_b(t) \\
\frac{M_0 b(t) - M_b(t)}{T_{1b}} & - (2\alpha - 1) \frac{\lambda}{\gamma} M_0 b(t) - \frac{\lambda}{\gamma} M_b(t) \\
\frac{M_0 b(t) - M_b(t)}{T_{1b}} & + \frac{\lambda}{\gamma} M_0 b(t) - \frac{\lambda}{\gamma} M_b(t)
\end{cases}
\]

\[
\text{when } t < \delta \\
\text{when } \delta \leq t \leq \tau \\
\text{when } \tau \leq t \leq \tau + \delta \\
\text{when } \tau + \delta \leq t \leq \tau + w
\]